REMARKS

A. Amendments in the specification

The abstract is amended, as requested by the Examiner, to a single paragraph in narrative form ranging from 50 to 150 words. No new matter is added by this amendment.

Further, as requested by the Examiner, Applicant states that no new matter was added by the March 7, 2007 amendment to the specification and requests entry of that amendment (Amendment C).

B. Amendments in the claims

The following claims are now pending in the present application: Claims 1–13. Claim 7 is withdrawn for examination purposes as being directed to non-elected subject matter. Six dependent claims (Claims 8–13) are added but the total number of claims remains not greater than 20. No excess claim fees are believed payable.

Claim 1 is amended to delete the phrase "and optionally at least one crystallization inhibitor"; this deletion is made to enhance clarity and will be seen to have no effect on scope of the claim as the previously recited component is optional.

Claims 1, 2, 4 and 5 are amended to provide clearer antecedent basis, as suggested by the Examiner.

New Claims 8 and 9, reciting crystallization inhibitors, find support in the specification as filed at least at page 12, lines 1–12 (corresponding to paragraph **[0059]** of the application as published under US 2005/0079206).

New Claims 10 and 11, reciting ranges of number of microreservoirs, find support in the specification as filed at least at page 6, lines 11–14 (corresponding to paragraph **[0035]** of the application as published).

New Claim 12, reciting a maximum diameter of the microreservoirs of 35 μm, finds support in the specification as filed at least at page 7, lines 26–27 (corresponding to paragraph **[0040]** of the application as published).

New Claim 13, reciting that the maximum diameter of the microreservoirs is 2.5 to 30 μm, finds support in the specification as filed at least at page 7, lines 22–27 (corresponding to paragraph **[0040]** of the application as published), where an exemplary matrix thickness of 50

μm and a preferred maximum size of 5% to 60% of the thickness of the matrix (*i.e.*, 2.5 to 30 μm) are disclosed.

Opportunity has been taken, in amending the claims, to correct typographical errors, to rephrase where it has been desirable to do so for enhanced clarity, and to present subject matter where necessary in terms more in accordance with standard U.S. claim drafting practice.

No new matter is added, and no change in inventorship is believed to result from amendment of the claims as proposed herein.

RESPONSE TO OFFICE ACTION DATED AUGUST 17, 2007

1. Objection to the abstract

The abstract is objected to as not being in narrative form and not limited to a single paragraph ranging from 50 to 150 words. By amendment herein, the abstract is now compliant. Applicant respectfully requests withdrawal of this objection.

2. Rejection under 35 U.S.C. §112, second paragraph

Claims 1–6 stand rejected under 35 U.S.C. §112, second paragraph, as indefinite for allegedly failing to particularly point out and distinctly claim subject matter which applicant regards as the invention. This rejection is respectfully traversed.

2.1. Definiteness of "optionally at least a crystallization inhibitor"

Claims 1–6 are rejected as vague and indefinite for allegedly not clearly specifying what condition would require "optionally at least a crystallization inhibitor". Claim 1 (from which Claims 2–6 directly or indirectly depend) is amended herein to delete the phrase "and optionally at least one crystallization inhibitor". Thus, the present ground of rejection is now moot.

2.2. Definiteness of "crystallization inhibitor"

Claims 1–6 are rejected for allegedly not clearly defining the term "crystallization inhibitor". As noted above, Claim 1 (from which Claims 2–6 directly or indirectly depend) is amended herein to delete the phrase "and optionally at least one crystallization inhibitor". Therefore, the present rejection with respect to Claims 1–6 is moot. However, new Claims 8

and 9 (which depend directly or indirectly from Claim 1) recite an embodiment of the invention wherein the microreservoirs additionally contain at least one crystallization inhibitor. In the interest of a full response, Applicant takes the opportunity to traverse the present rejection with regard to new Claims 8 and 9.

Under MPEP 2173.01, a claim term that is not defined is not indefinite if the meaning of the claim term is discernible. The Examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope. Applicant submits that one of ordinary skill in the art would clearly understand the meaning of "crystallization inhibitor," especially in light of the present specification, which provides at page 12, lines 1–12 (corresponding to paragraph **[0059]** of the application as published), that several surfactants or amphiphilic substances may be used as crystallization inhibitors and further provides specific examples of suitable crystallization inhibitors. Therefore, one of skill in the art would understand, after reading the specification, what it is meant by the term "crystallization inhibitor."

Furthermore, Claims 8 and 9 recite specific crystallization inhibitors (a Markush group in Claim 8, and a specific crystallization inhibitor in Claim 9). Under these circumstances, the meaning of the term "crystallization inhibitor" as used in Claims 8 and 9 is clearly not indefinite.

2.3. Definiteness of "a multitude of microreservoirs"

Claim 1 is rejected as indefinite because it is allegedly not clear what is meant by the term "a multitude of microreservoirs." The word "multitude" is used in its ordinary dictionary sense of "a great number" and therefore one of skill in the art would clearly understand that "a multitude of microreservoirs" as recited in Claim 1 means a great number of microreservoirs. It is a number that clearly comprises, without limitation, the "preferred" range of 10^3 to 10^9 per cm^2 disclosed at page 6, line 12 of the specification as filed (corresponding to paragraph **[0035]** of the application as published). Fig. 5 of the present application provides a vivid pictorial image of a multitude of microreservoirs.

The term "multitude" is widely accepted as a descriptor of a large plurality in U.S. claim writing practice. A search of the USPTO Full-text Patent and Image Database (all U.S.

patents issued since 1976) returns no fewer than 2,722 patents in which the word "multitude" appears in at least one claim, yet Applicant has been unable to find a single case in which a question of invalidity has turned on indefiniteness of this word. The synonym "multiplicity" is even more universally accepted, appearing in at least one claim of no fewer than 22,705 U.S. patents issued since 1976.

In view of the above showing, it is Applicant's position that the expresssion "a multitude of microreservoirs" is not indefinite. The present ground of rejection is therefore respectfully traversed.

2.4. Definiteness regarding "the mean diameter of the microreservoirs"

Claim 2 is rejected as indefinite because it allegedly lacks proper antecedent basis. By amendment of Claim 2 herein, the present ground of rejection is now moot.

Although the issue is moot, Applicant respectfully draws the Examiner's attention to MPEP 2173.05(e), stating: "Inherent components of elements recited have antecedent basis in the recitation of the components [for which read 'elements'] themselves. For example, the limitation 'the outer surface of said sphere' would not require an antecedent recitation that the sphere has an outer surface." In the present case, "the mean diameter" is an inherent feature of microreservoirs, thus antecedent basis was present in Claim 2 as originally worded.

2.5. Definiteness regarding "the polymer matrix"

Claims 4 and 5 are rejected as indefinite because the term "the polymer matrix" allegedly lacks proper antecedent basis. Claims 4 and 5 are amended herein, as suggested by the Examiner, to recite "the self-adhesive matrix". Thus, this rejection is rendered moot by the present amendment.

2.6. Rejection under 35 U.S.C. §112, second paragraph: general remarks

In light of the showing above, withdrawal of all rejections under 35 U.S.C. §112, second paragraph is respectfully requested.

3. Rejection under 35 U.S.C. §103(a)

Claims 1–6 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Mantelle *et al.* (U.S. Patent No. 6,316,022, herein "Mantelle") in view of Brecht (U.S. Patent

Application Publication No. 2001/0053777, herein "Brecht"), Rossi-Montero *et al.* (U.S. Patent No. 6,465,004, herein "Rossi-Montero"), Sackler *et al.* (U.S. Patent No. 5,733,571, herein "Sackler") and Mueller *et al.* (U.S. Patent No. 6,884,434, herein "Mueller II"). This rejection is respectfully traversed.

No admission is made herein that any of the cited documents constitutes prior art to the present invention. It is noted that Mueller II is not statutory prior art against the present invention, having issued after the priority date of the present application. However, Mueller II derives from a national phase filing of PCT/EP99/01795, which published earlier than Mueller II as WO 99/49852 (herein "Mueller I") and discloses at page 1, lines 9–10, (–)-5,6,7,8-tetrahydro-6-propyl[2-(2-thienyl)ethylamino]-1-naphthol, the structure of which corresponds to rotigotine.

To reach a proper determination under 35 U.S.C. §103, the Examiner must step backward in time and into the shoes worn by the hypothetical "person of ordinary skill in the art" when the invention was unknown and just before it was made. In view of all factual information, the Examiner must then make a determination whether the claimed invention "as a whole" would have been obvious at that time to that person. Knowledge of Applicant's disclosure must be put aside in reaching this determination. MPEP 2142. According to the present Action, five documents are combined in order to arrive at the present ground of rejection. Such combination can only be made, impermissibly, by hindsight reconstruction of the invention based on the disclosure of the present specification. Applicant submits that, at least for this reason, a *prima facie* case of obviousness has not been established.

However, even if it is determined that impermissible hindsight was not used to combine these five documents (which is not admitted herein), a rationale for combining references must come from logic and sound scientific reasoning. MPEP 2144(I). Here, the Examiner's rationale is that based on the teachings of Mantelle, the primary reference, one of skill in the art would have been motivated to combine the references to take advantage of the reduced loss of free base drug in the TDS during manufacture. Applicant respectfully submits that this rationale is erroneous, as sound scientific reasoning would not lead to the cited combination of references. Specifically, the stated rationale for combining the references fails

because the primary reference discusses reduction of loss of drugs which are liquid at or about room temperature. Rotigotine is not a liquid at room temperature, thus one of skill in the art would not have been motivated to combine the teachings of Mantelle with references teaching use of rotigotine. Therefore, because no proper motivation or suggestion to combine or modify the references has been articulated, a *prima facie* case of obviousness has not been established.

Moreover, all claim limitations must be considered in judging the patentability of a claim against the prior art. MPEP 2143.03. Even if a sound rationale for combining the references had been provided (which is not admitted herein), the resulting combination fails to teach or suggest all claim limitations. If the references are missing claimed features, there must be some apparent reason either in the references or the general knowledge in the art to modify the references to include the missing subject matter. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740-41, 82 USPQ2d 1385, 1396 (2007).

According to Claim 1 as amended herein, the self-adhesive matrix comprises within the matrix a multitude of microreservoirs, said microreservoirs containing rotigotine and having a maximum diameter that is less than the thickness of the matrix. The primary reference, Mantelle, fails to disclose a multitude of microreservoirs, and fails to disclose microreservoirs having a maximum diameter meeting the criteria of Claim 1.

Mantelle contemplates various types of transdermal drug delivery system (*e.g.*, a reservoir device or an adhesive monolithic device). The present Action construes the "multitude of microreservoirs" previously recited in Claim 1 as being coextensive with the reservoir embodiment of Mantelle. Applicant respectfully disagrees with this construction. Nowhere does Mantelle suggest that the reservoir embodiment of Mantelle is subdivided into a multitude of microreservoirs. The "multitude of microreservoirs" recited in Claim 1 is not only non-coextensive with Mantelle's reservoir, it does not even embrace any reservoir system disclosed by Mantelle. According to the present specification at page 6, lines 7–14 (corresponding to paragraph **[0035]** of the specification as published), "microreservoirs" are defined as particulate, spatially and functionally separate compartments consisting of pure drug or a mixture of drug and crystallization inhibitor, which are dispersed in the self-

adhesive (polymer) matrix. By contrast, nothing in Mantelle teaches or suggests dispersion of reservoirs, particularly a multitude of microreservoirs, dispersed within a self-adhesive polymer matrix, such microreservoirs having a maximum diameter that is less than the thickness of the matrix.

None of the secondary references (Brecht, Rossi-Montero, Sackler or Mueller I) is found to supply the missing feature, thus no combination of the cited documents teaches or suggests all the claim limitations, and accordingly for at least this reason a *prima facie* case of obviousness has not been established.

Applicant respectfully disagrees with the Examiner's remark that additional elements recited in Claim 1, namely "wherein the self-adhesive matrix comprises a solid or semi-solid semi-permeable polymer," "substantially impermeable to the protonated form of rotigotine," and "wherein the maximum diameter of the microreservoirs is less than the thickness of the matrix," are "reasonably construed to be coextensive features of the TTS [*i.e.*, TDS] matrix, absent evidence to the contrary" (Action, bottom of page 11). Each of these elements can be present in a TDS matrix independent of the others, but presence of all of them is a requirement of Claim 1. In particular, as taught in the specification, it is an important feature that a matrix be chosen that is substantially impermeable to rotigotine in its protonated or salt form. See, for example, at page 2, lines 26–33 of the specification as filed, wherein an objective of the present invention is stated to be "... enhanced delivery of rotigotine to and across the skin by ... preventing back diffusion of the drug portion which is ionized in the skin according to its pKa value – from the skin tissue into the TDS ..." (emphasis added). It is likewise an important feature that the microreservoirs have a maximum diameter less than the thickness of the matrix, so as to minimize direct contact between the skin and the microreservoirs, which would result in back diffusion of protonated rotigotine from the skin into the microreservoirs. See, for example, at page 8, lines 1–10 of the specification as filed.

Notwithstanding the Examiner's remarks with respect to Claims 2–6, these claims each embody all the limitations of Claim 1 from which they depend or which they reference, and are therefore nonobvious at least for the same reasons that Claim 1 is nonobvious. If an independent claim is nonobvious under 35 U.S.C. §103, then any claim depending therefrom

is nonobvious. MPEP 2143.03.

Withdrawal of the present rejection under 35 U.S.C. §103(a) is respectfully requested for the reasons given above.

4. Provisional double patenting rejection

Claims 1–6 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 5–16 of copending application Serial No. 10/429,283, in view of Brecht (U.S. Patent Application Publication No. 2001/0053777) and over Claims 1–13 of copending application Serial No. 10/627,990, in view of Brecht. The rejection is provisional because the allegedly conflicting claims have not yet been patented. Applicant may elect to argue to overcome this ground of rejection or to provide a terminal disclaimer (to the extent necessary) once the present claims have been found to be otherwise allowable and/or once the '283 or '990 applications issue as patents.

5. Rejection under 35 U.S.C. §112, first paragraph

Claims 1–6 stand rejected under 35 U.S.C. §112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner acknowledges that the disclosed examples of crystallization inhibitors have met the written description and enablement provisions of 35 U.S.C. §112, first paragraph. However, the Examiner states that Claims 1–6 are allegedly directed to non-disclosed crystallization inhibitors which only correspond in some undefined way to specifically instantly disclosed chemicals. The Examiner argues that these non-disclosed crystallization inhibitors fail to meet the written description provision of 35 U.S.C. §112, first paragraph, due to lacking chemical structural information. Applicant has amended Claim 1 to delete "and optionally at least a crystallization inhibitor", therefore the present rejection of Claim 1 and Claims 2–6 (which either directly or indirectly depend from Claim 1) is moot. With respect to new Claims 8 and 9, which recite crystallization inhibitors, the present ground of rejection is also moot, because no "non-disclosed" crystallization inhibitors are embraced by these claims.

Although the issue is moot as indicated above, Applicant respectfully draws the

Examiner's attention to the strong presumption that an adequate written description of the claimed invention is present when the application is filed. MPEP 2163(I)(A). The objective standard set forth in MPEP 2163.02 for determining compliance with the written description requirement is whether "the description clearly allows persons of ordinary skill in the art to recognize that he or she invented what is claimed." Not only does the specification provide specific examples of suitable crystallization inhibitors, but the art is replete with examples of compounds useful as crystallization inhibitors. Illustratively, a search of U.S. patents issued since 1976 in the USPTO database retrieves no fewer than 201 patents mentioning the term "crystallization inhibitor" in the specification. Applicant submits that through the examples provided in the specification and the general knowledge in the field, one of ordinary skill, on reading the specification together with the claims, would know what is meant by the term "crystallization inhibitor" without further structural definition.

Withdrawal of the present rejection under 35 U.S.C. §112, first paragraph is respectfully requested.

6. Conclusion

It is believed that all of the stated grounds of rejection are properly traversed, accommodated or rendered moot herein. Applicant therefore respectfully requests that the Examiner reconsider and withdraw all presently outstanding rejections. It is believed that a full and complete response has been made to the present Action and that the Application is in condition for allowance.

If personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number below.

Respectfully submitted,

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